

Applicant: Zeppezauer et al.
Serial No.: 09/988,165

Amendments to the Specification

On page 3, please replace the paragraph beginning on line 14 with the following rewritten paragraph:

- (1₁) KPKAA KPKAA KPKAA KPKKA APKKK, (SEQ ID NO. 1)
(1₂) KPKAA KAR~~U~~V~~T~~ KPKTA KPKKA APKKK (SEQ ID NO. 4)
(1₃) AAKAV KPKAA KPKVV KPKKA APKKK (SEQ ID NO. 5)
(1₄) KPKAA KPKSG KPKVT KAKKA APKKK (SEQ ID NO. 6)
(1₅) KPKAA KPKTA KPKAA KPKAA AAKKK (SEQ ID NO. 7)
(1₆) KPKAA KPKAA KPKAA KAKKA AAKKK (SEQ ID NO. 8)
(1₇) KPKAA KPKAA KPKAA KP KAKKA AAKKA (SEQ ID NO. 9)
(2) PEPAP SAPAP KKGSK KAVTK AQKKD GKRRK RSEKE, (SEQ ID NO. 2) and
(3) SYSVY VYKVL KQVHP DTGIS SKAMG IMNSF VNDIF ERIAGE (SEQ ID NO. 3). --

On page 4, please replace the section beginning on line 1 with the following rewritten section:

-- Histon-H1-Peptide (bovine peptides)

H1-N-Terminus : 3 – 29

APAAP AAAPP AEKTP VKKKA AKK

PA GA (SEQ ID NO. 10)

H1: 55 – 75

RSGVS LAALK KALAA AGYDVE (SEQ ID NO. 11)

H1: 97 – 116

TKGTG ASGSF KLNKK AASGE (SEQ ID NO. 12)

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H1: 76 – 116

KNNS RIKLG LKSLV SKGTL VETKG
TGASG SFKLN KKAAS GE (SEQ ID NO. 13)

H1: 66 – 116

ALAA AGYDV EKNNS RIKLG LKSLV
SKGTL VETKG TGASG SFKLN KKA
SGE (SEQ ID NO. 14)

H1: 55 – 116

RSGVS LAALK KALAA AGYDV EKNNS
RIKLG LKSLV SKGTL VETKG TGASG
SFKLN KKAAS GE (SEQ ID NO. 15)

H1-C-Terminus : 187-211

KPKAA KPKAA KPKAA KPKKA APKKK (SEQ ID NO. 16) --

On page 4, please replace the section beginning on line 30 with the following
rewritten section:

-- Histon H2B-Peptide (bovine or human peptide)

H2B: 1-35

PEPAK SAPAP KKGSK KAVTK AQKK
D GKRRK RSEKE (SEQ ID NO. 17)

H2B: 36-76

SYSVY VYKVL KQVHP DTGIS SKAMG
IMNSF VNDIF ERIAG E (SEQ ID NO. 18)

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H2: 77-93

ASRLA HYNKR STITS RE (SEQ ID NO. 19)

H2B: 94-105

IQTAV RLLLP GE (SEQ ID NO. 20)

H2B: 106-113

LAKHA VSE (SEQ ID NO. 21)

H2B: 113-124

GTKAV TKYTS SK (SEQ ID NO. 22)

H2B: N-Term. 1-21

PEPAK SAPAP KKGSK KAVTKA (SEQ ID NO. 23)

H2B N-Term: 4-11

AKSAPAPK (SEQ ID NO. 24)

Histon H2A-Peptide

H2A-N-Terminus

SGRGK QGGKA RAKAK TRSSR AG (SEQ ID NO. 25) --

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On page 5, please replace the section beginning on line 29 with the following rewritten section:

-- Histonsequenzen: (bovine or human peptide)

H2A:

SGRGK QGGKA RAKAK TRSSR AGLQF
PVGRV HRLLR KGNYA ERVGA GAPVY
LAAVL EYLTA ELLEL AGNAA RDNKK
TRIIP RHLQL AIRND EELNK LLGKV
TIAQG GVLPN IQAVL LPKKT ESHHK
AKGK (SEQ ID NO. 26) --

On page 6, please replace the paragraph beginning on line 8 with the following rewritten paragraph:

-- The inventors are also aware that the amino acid sequences of the C terminal parts of the histone H1 subtypes of human and as far as they are known of consensus sequences, i.e., bovine and other mammals are very similar. They are composed of homologous sequence patterns (boxes) of the type KPAAA (SEQ ID NO. 27), KPAAA (SEQ ID NO. 28), KAKKA (SEQ ID NO. 29) or boxes derived from them by exchange of one or two amino acids. --

On page 6, please replace the paragraph beginning on line 14 with the following rewritten paragraph:

-- The final box is APKKK (SEQ ID NO. 30) or AAKKK (SEQ ID NO. 31). --

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On page 6, please replace the section beginning on line 19 with the following rewritten paragraph:

-- Histon-H1-Peptide (human peptide)

H1.1: 191-215

KPKAA KARUVT KPKTA KPKKA APKKK (SEQ ID NO. 4)

H1.2: 193-218

AAKAV KPKAA KPKVV KPKKA APKKK (SEQ ID NO. 5)

H1.3: 195-220

KPKAA KPKSG KPKVT KAKKA APKKK (SEQ ID NO. 6)

H1.4: 191-216

KPKAA KPKTA KPKAA KPKAA AAKKK (SEQ ID NO. 7)

H1.5: 195-225

KPKAA KPKAA KPKAA KAKKA AAKKK (SEQ ID NO. 8)

H1.a: 195-222

KPKAA KPKAA KPKAA KP KAKKA AAKKA (SEQ ID NO. 9) --

On page 7, please replace the paragraph beginning on line 1 with the following rewritten paragraph:

-- From the peptides 1₁ til 1₇ smaller peptides may be selected which contain at least eight amino acids and at least one consensus sequence (depicted as boxes of five amino acids) whereby the C terminal is always AXKKK (SEQ ID NO. 32) (X=A or P). --

On page 11, please replace the paragraph beginning on line 29 with the following rewritten paragraph:

-- The invention also comprises the use of the peptides of the invention in the therapy of immunological disorders, in particular of SLE, rheumatoid arthritis and sclerodermia. In the therapeutical methods of the invention a pharmaceutical composition which comprises a therapeutically effective amount of at least one peptide with an amino acid sequence as disclosed herein in SEQ ID NO. 1, 2, ~~or~~ 3, 4, 5, 6, 7, 8, or 9 is administered to a patient. A therapeutically effective amount of a peptide is an amount which upon single or repeated administration to a patient does alleviate an inflammation or reduce any symptom of the aforementioned disorders. The pharmaceutical compositions of a first embodiment of the invention comprise at least one lyophilised peptide of SEQ ID NO. 1 to ~~3~~ 9 in dry form, which can be readily dissolved, *e.g.*, in phosphate-buffered saline (PBS), aqua ad injectabilia, Ringer's solution or the like, prior to use. The pharmaceutical compositions may also comprise pharmaceutically acceptable carriers. The pharmaceutical preparations are preferably administered by parenteral injection, renal perfusion, or by oral application. The pharmaceutical compositions of the invention are specialised embodiments adapted to various oral or topical applications to a patient. The skilled in the art readily prepares the suitable compositions. The pharmaceutically effective amount of a single dose of at least one peptide of the invention depends on the age and size of the patient, on the route of administration, and the severeness of the symptoms. Without any restriction, a therapeutically effective amount of a peptide may range from 0.1 to several hundred milligrams. In an advantageous embodiment, the pharmaceutical composition comprises the peptides of SEQ ID No. 1, 4, 5, 6, 7, 8 or 9 and SEQ ID NO. 2 in equimolar amounts.

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